REMARKS

Claims 1 and 3-26 stand rejected. Claims 3-4, 17-18 and 20 have been cancelled. Claims 1, 5, 6, 8, 11, 13-16 and 21-26 have been amended. Support for the amendments can be found throughout the specification, specifically paragraphs 23-36 and 37-52 inclusive. Claims 1, 5-16, 19 and 21-26 are therefore now pending.

I. Priority:

The Examiner alleges that a certified copy of the priority document EP 02019100.3, filed August 29, 2002 is missing and that the conditions of 35 USC 119 (a-d) have not been met. Applicants note for the record that a certified copy of the priority document (EP 02019100.3, filed August 29, 2002) was supplied to the Patent and Trademark Office on March 22, 2004. Applicants herein attach a copy of the March 24, 2004 postmarked receipt from the Patent and Trademark Office evidencing said submittal and also herein attach another copy of the priority document for the Examiner's file. Accordingly, Applicants respectfully submit that the conditions of 35 U.S.C. 119 (a-d) have been met.

II. Duplicate Claims Warning:

Claims 3-12 and 17-26 are asserted to be substantially duplicative. Applicants have cancelled claims 17-18 and 20 and amended claims 19 and 21-26. Applicants respectfully submit that the claims as now presented are not duplicative of each other and that, accordingly, the duplicative claim warning/objection is obviated and should be withdrawn.

III. Claim Rejections

A. 35 USC 112, first paragraph

1. Claims 1, 3, 5-17 and 19-26 stand rejected by the Examiner under 35 USC 112, first paragraph for lack of written description. Specifically, the Examiner contends that the claims encompass fragments (analogs) and alleges that the specification does not

demonstrate retention of function for the fragments to demonstrate possession of the genus as claimed in the invention. Applicants respectfully traverse.

With regard to Claims 1, 3, 5-17 and 19-26, as amended, Applicants respectfully wish to point out that each claim specifically describes and identifies the protein or analogs claimed, with reference to words, structures and formulae that fully set forth the claimed invention (*Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). For example, Claims 1, 5, 6, 8, 11, 16, 19, 22 and 25 specifically recite or depend upon a reference structure (SEQ ID NO:1) for the claimed protein, with Claim 5 specifically listing the modification sites with reference to the reference structure and Claim 6 listing specific analogs of the protein. In addition, Claims 8-12 specifically set forth the limit of said ranges for each of the component parts of the conjugate of the reference structure and its molecular weight and its activity. Support for these claims are found generally throughout Applicants' specification and specifically with regard to paragraphs 23-36 inclusive, and paragraphs 37-52 inclusive demonstrate and describe how to produce said conjugates as claimed. The Examiner acknowledges that the species are adequately described. As the species have included unpegylated and pegylated erythropoietin conjugates, 1-6 glycosylation sites and erythropoietin conjugates with 1-6 glycosylation sites (as depicted in various formula in the specified paragraphs above, as well as methods for making same) collectively hereinafter referred to as "EPO stimulating agents" or "ESA" of the invention, Applicant respectfully submits that the genus has been sufficiently described and disclosed in drawings/structural formula to show Applicant's possession of the claimed genus and thus also, the claimed invention.

2. Claims 13-15 also stand rejected under 35 U.S.C. 112, 1st paragraph. The Examiner views the claimed pharmaceutical compositions, without the recitation of a pharmaceutically acceptable carrier or excipient therein, as lacking adequate written description. The Examiner alleges that the pharmaceutical composition requires a pharmaceutically acceptable carrier. Applicants respectfully traverse.

The "essential goal" of the written description requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed." In re Barker, 559 F2d 588, 592, n4, 194 USPQ 470, 473, n.4 (CCPA 1577) To satisfy the written description requirement, the applicant's specification must reasonably convey to those skilled in the art that the applicant was in possession of the claimed invention as of the date of the invention. Regents of the University of California v. Eli Lilly, 119 F3rd 1559, 1566, 43 USPQ 2d 1398, 1404 (Fed. Cir. 1997), cert denied, 523 US 1089 (1998).

"There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." MPEP 2163, *In re Wertheim*, 541 F20257, 263, 191 USPQ 90, 97 (CCPA 1976)." The Examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the disclosure a description of the invention as defined by the claims." MPEP 2163.04.

Applicants herein have amended claim 13 (and independent claims 14 and 15) to recite "a composition for the treatment of ...." thereby obviating the rejection.

Applicants note for the record that the claimed compositions do describe the conditions and make up of said compositions, including the pH of the composition, the amount of EPO, and at least one other component (sulfate, mannitol, methione, poloxamer) – with each such component and EPO described in ranges or approximations of mass/weight per unit volume. One skilled in the art could readily use these parameters to practice the claimed compositions.

Applicants therefore respectfully submit that its specification and the claimed compositions of claims 13-15 as currently presented do indeed reasonably convey the invention to one of ordinary skill in the art. Accordingly, Applicants respectfully submit that claims 13-15 as currently presented are in condition for allowance.

35 USC 112, first paragraph

Claims 1, 3, 5-17 and 19-26 stand rejected by the Examiner under 35 USC 112, first paragraph, for lack of enablement. Specifically, the Examiner contends that the specification, while being enabling for the method of treating disturbances in iron distribution, does not provide enablement for the use of analogs of EPO (protein) in said method. The Examiner contends that the claims encompass an unspecified number of analogs, unlimited free amino groups and no structure of the EPO protein used in the claimed method.

With regard to Claims 1, 3, 5-17 and 19-26, as amended, Applicants respectfully wish to point out that each claim specifically describes and identifies the protein or specific analogs claimed, with reference to words, structures and formulae that fully set forth the claimed invention (*Lockwood v. American Airlines, Inc.,* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997) so that one of ordinary skill in the art could practice the claimed invention. Claims 1, 5, 6, and 13 for example specifically recite or depend upon a reference structure (SEQ ID NO:1) for the claimed protein, with Claim 5 specifically listing the modification sites with reference to the reference structure and Claim 6 listing specific analogs of the protein. In addition, Claims 8-12 specifically set forth the limit of said ranges for each of the component parts of the conjugate of the reference structure and its molecular weight and its activity. Support for these claims are found generally throughout Applicants' specification and specifically with regard to paragraphs 23-36 inclusive, and paragraphs 37-52 inclusive demonstrate and describe how to produce said conjugates as claimed. The Examiner acknowledges that the species are adequately described and enabled. As the described and enabled species have included the "ESA" of the invention (as depicted in various formula in the specified paragraphs above, as well as methods for making same), Applicant respectfully submits that the genus has been sufficiently described and disclosed in drawings/structural formula, as well as depicting a specified amount of analogs, a specified range on the number of amino groups, to enable a skilled artisan to practice

the invention as presently claimed. Accordingly, Applicants respectfully submit that the invention as claimed within claims 1-2 and 5-14 is enabled and thus the 112 rejection is overcome.

B. 35 USC 112, second paragraph

1. Claims 3-15 and 17-26 apparently stand rejected for alleged failure to set forth and claim the subject matter which applicants regard as their invention. The Examiner has rejected claims 3-15 and 17-26 for lack of clear antecedent basis for "the erythropoietin protein" as original claim 1 recites "human erythropoietin".

Applicants have amended Claims 5,6,8, 11, 13-15, 22, 25 to reflect "human erythropoietin protein", thus providing antecedent support for claims dependent therein and obviating the rejection. Accordingly, Applicants respectfully submit that claims 5-15 and 17-26 as currently presented are now in condition for allowance.

2. Claims 5 and 19 are asserted to lack clear antecedent basis for 'human erythropoietin modified by the additional of from 1 to 6 glycosylation sites" as independent claim 1 is directed to "human erythropoietin protein". Applicants have amended claims 5 and 15 to be independent. Accordingly, Applicants respectfully submit that the rejection has been obviated and that claims 5 and 19 are now in condition for allowance.

3. Claims 8-12 and 22-26 stand additionally rejected for lack of clear antecedent basis for the phrase "the erythropoietin protein is a conjugate" as original claim 1 recites "human erythropoietin".

As noted above, Applicants have amended now independent Claims 8, 11, 22 and 25 to reflect "... administering a conjugate of human erythropoietin of SEQ ID NO:1.", thus providing antecedent support claims dependent thereon (9-10, 23-24) and

thus obviating the ground of the rejection for these claims. applicants respectfully submit that claims 8-12 and 22-26 are in condition for allowance.

4. Claims 13-15 also stand rejected under 37 USC 112, 2nd paragraph. The Examiner alleges that the recitation of a pharmaceutical composition, without a recitation of a carrier, renders the claims indefinite. Applicants traverse and respectfully reiterate the above 112, first paragraph response here as well.

As noted in the MPEP § 2171, whether a claim is indefinite under 112, 2nd paragraph is "evaluated in the context of whether the claim is definite – i.e., whether the scope of the claim is clear to a hypothetical person possessing the ordinary level of skill in the pertinent art." Section 2173 states that "(t)he primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent." An "applicant may use functional language, alternative expressions, negative limitations, or any style of expression or format of claim which makes clear the boundaries of the subject matter for which protection is sought. As noted by the court in *In re Swinehart*, 439 F.2d 210, 160 USPQ 226 (CCPA 1971), a claim may not be rejected solely because of the type of language used to define the subject matter for which patent protection is sought." (2173.01)

Accordingly, "(i)n reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, "by providing clear warning to others as to what constitutes infringement of the patent". See, e.g, *Solomon v. Kimberly-Clark Corp.*, F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 20000). See also *In re Larsen*, No. 01-1092 (Fed. Cir. May 9, 2001) (unpublished) (The preamble of the *Larsen* claim recited only a hanger and a loop but the body of the claim positively recited a linear member. The court observed that the totality of all the

limitations of the claim and their interaction with each other must be considered to ascertain the inventor's contribution to the art. Upon review of the claim in its entirety, the court concluded that the claim at issue apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112 paragraph 2.)."

In the claims at issue, the claimed compositions comprise and recite a specific range of mass/volume of erythropoietin protein (ESA), and at least one other component in a specified range for each component (in mass or weight/volume) as well as a specified pH range or approximate level. For example, claim 13 recites:

"A composition for the treatment of disturbances in iron distribution comprising from about 25 to about 2,500 μg/ml of erythropoietin protein, from about 10 to about 200 mmol/l sulfate and having a pH of from about 6.0 to about 7.0.

The test for definiteness under 35 U.S.C. 112, second paragraph, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification. "*Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). Applicants respectfully submit that one of ordinary skill in the art would understand the scope of Applicants' composition claims 13-15, as amended.

Accordingly, Applicants respectfully submit that the rejection to claims 13-15 as amended is inappropriate and thus said claims are in condition for allowance.

D. 35 USC 102(a)

Claims 1, 3-4 and 17-18 stand rejected under 35 U.S.C. 102(a) as being allegedly anticipated by Silverberg et al. (Nephrol. Dial. Transplant, vol. (18)1, pages 141-146, 2003).

Silverberg et al. is asserted as disclosing a treatment of correcting anemia with subcutaneous EPO with Type II diabetes. Applicants respectfully traverse.

Applicants invention claims priority back to the August 29, 2002 filing date in Europe. (See specification, page 1, see certified copy of earlier claimed filing and date thereof submitted to USPTO on March 24, 2004). As this 2002 filing date pre-dates the cited Silverberg reference, the Silverberg reference is not prior to Applicants' invention. As such, the 102(a) rejection is inappropriate. Accordingly, Applicants respectfully submit that the 102(a) rejection be withdrawn and that claim 11 is in condition for allowance.

E. 103(a) Rejection

Claims 1, 4-15 and 18-26 are rejected under 35 USC 103(a) as being obvious over Silverberg et al in view of Hoffmann-La Roche (EP 1064951, 1/3/01). Silverberg is again asserted as disclosing a treatment of correcting anemia with subcutaneous EPO in patents with Type II diabetes. Silverberg is acknowledged as not teaching EPO with modifications such as glycosylation of 1-6 or pegylated erythropoietin conjugates. The '951 patent is asserted to teach glycosylation of erythropoietin and pegylated erythropoietin conjugates.

However, as noted ante, Applicants invention has a priority date of August 29, 2002, which pre-dates the Silverberg reference. As such, the Silverberg reference is not prior art as to Applicants invention and thus fails as a 103(a) reference. Accordingly, applicants respectfully submit that the 103(a) rejection is inappropriate and should be withdrawn and claims 1, 5-6, 8, 11-16 and 21-26 are in condition for allowance.

F. The Double Patenting Rejection

Claims 1, 3-15 and 17-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 3-14 of copending application USSN 10/706,701. As claims 1 and 3-12 of USSN

10/706,701 are not allowed, applicants respectfully submit that this rejection is premature. Furthermore, as amended claims 1, 56-, 8, 11-16 and 21-26 herein do not require the absence of iron in said claimed methods, Applicants respectfully submit that these claims are patentably distinct over claims 1 and 3-14 of USSN 10/706,701, which does not require the absence of iron in its claimed methods. Accordingly, Applicants respectfully request the Examiner to withdraw the double patenting rejection.

Claims 1, 3-12 and 17-26 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 4-15 of copending application USSN 11/013,560. As claims 1 and 4-15 of USSN 11/013,560 are not allowed, applicants respectfully submit that this rejection is premature. Furthermore, as amended claims 1, 5-6, 8, 11-16 and 21-26 herein do not require the absence of iron in said claimed methods, Applicants respectfully submit that those claims over claims 1 and 4-15 of USSN 11/013,560 which does require the absence of iron in tits claimed methods. Accordingly, Applicants respectfully request the Examiner to withdraw the double patenting rejection.

CONCLUSION

The foregoing amendment is fully responsive to the Office Action issued March 13, 2006. Applicants submit that claims 1, 5-6, 8, 11-16 and 21-26, as amended, are allowable. Early and favorable consideration is earnestly solicited.

If the Examiner believes there are other issues that can be resolved by telephone interview, or that there are any informalities remaining in the application which may be corrected by Examiner's Amendment, a telephone call to the undersigned attorney is respectfully solicited.

No further fee is required in connection the filing of this Amendment. If any additional fees are deemed necessary, authorization is given to charge the amount of any such fee to Deposit Account No. 08-2525.

Respectfully submitted,

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